Age-related changes to the expression of nuclear factor erythroid 2-like 2 (Nrf2), a regulatory antioxidant and xenobiotic defence gene

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Introduction Multimorbidity, polypharmacy and susceptibility to adverse drug reactions (ADR) are common problems in old age. Understanding the age-related biological changes that occur at a cellular level, may assist in identifying novel therapeutic targets. The nuclear factor erythroid 2-like 2 (Nrf2) transcription factor regulates antioxidant and drug metabolising pathways in the cell. Data from rodent models showed that Nrf2 protein expression declines with age. If similar findings are observed in humans, it may help to explain why older people are vulnerable to multimorbidity and ADRs. This study investigates whether Nrf2 expression (both mRNA and protein) decreases with increasing age in humans.

Methods Fifty-five adults were recruited to our study (age range: 18-75 years). Participants donated 6 mL of venous blood, from which peripheral blood mononuclear cells (PBMCs) were separated and analysed for Nrf2 mRNA and protein expression (real time quantitative polymerase chain reaction and enzyme-linked immunosorbant assay respectively).

Results Our data showed that Nrf2 protein expression was approximately 50% lower in individuals aged >30 years (0.065 ±0.014 EU <30 years vs. 0.033 ±0.0060 EU >30 years, $p<0.05$). Similarly, mRNA expression declined with advancing age (log_2-fold change compared to 18-29 year-olds: 1.08±1.19, 2.14±1.25, -0.69±1.15, 0.45±2.03, -4.76±2.06, in 30-39, 40-49, 50-59, 60-69, >70 year age categories respectively; $p<0.0001$).

Conclusions The expression of Nrf2 transcription factor is reduced in old age, potentially contributing to the increased risk of multimorbidity and adverse drug reactions.